UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/819,308	03/27/2001	Mathieu Hubertus M. Noteborn	4820US	4047

24247 7590 12/04/2002

TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER	
WOITACH, JOSEPH T	
ART UNIT	PAPER NUMBER
1632	10

DATE MAILED: 12/04/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/819,308	Noteborn et al.
Examiner	**Art Unit**
Joseph Woitach	1632

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) X Responsive to communication(s) filed on *Sep 6, 2002* .

2a) ☐ This action is **FINAL**. 2b) X This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) X Claim(s) *15, 16, and 19-21* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) X Claim(s) *15, 16, and 19-21* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) X Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) X All b) ☐ Some* c) ☐ None of:

1. X Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) X	Notice of References Cited (PTO-892)	4) ☐	Interview Summary (PTO-413) Paper No(s).
2) ☐	Notice of Draftsperson's Patent Drawing Review (PTO-948)	5) ☐	Notice of Informal Patent Application (PTO-152)
3) X	Information Disclosure Statement(s) (PTO-1449) Paper No(s). 5	6) ☐	Other:

DETAILED ACTION

This application filed March 27, 2001 claims benefit to foreign application 00201108.8 filed March 27, 2000 with European Patent Office.

Applicants' amendment filed September 6, 2002, paper number 9, has been received and entered. Claims 1-14, 17 and 18 have been canceled. Claims 15 and 19 have been amended. Claims 15, 16, 19-21 are pending and currently under examination.

Election/Restriction

Applicant's election with traverse of Group VIII in Paper No. 9 is acknowledged. The traversal is on the ground(s) that it would not be an undue burden to examine Group VII. Applicants point out that the sequences are related in the ability to induce apoptosis, and that a search conducted by the EPO has been also provided in the form of an IDS. Applicants argue that two sequences would not constitute an undue burden to search and examine both groups. Applicants' arguments have been fully considered and found persuasive. In particular, upon examination of the sequences homology comparisons of SEQ ID NO: 1 and SEQ ID NO: 9 indicate that SEQ ID NO: 1 is a partial clone of SEQ ID NO: 9. Examiner agrees that a search of SEQ ID NO: 9 would identify partial sequences as encompassed by SEQ ID NO: 1, and thus, would not constitute an undue burden. Therefore, the restriction requirement between groups VII and VIII is withdrawn.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claims 15, 16 and 19-21 are pending and currently under examination as they are drawn to a method of inducing apoptosis in a cell or a subject by administering either SEQ ID NO: 1 or SEQ ID NO: 9.

Information Disclosure Statement

The information disclosure statement filed May 31, 2001, paper number 5, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered.

Specifically, copies of two references, Zhao *et al.* and Strusberg (wd70d04.x1), are not present.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

Claims 15 and 19 are objected to because of the following informalities: both claims 15 and 19 recite "Apoptin-associating proteinaceous substance" and thus, encompass inventions restricted into Groups IX and X. It is noted that the polynucleotides can encode a Apoptin-associating protein, however the elected methods are drawn to delivering polynucleotides, not polypeptides. The claims should be amended to reflect the elected invention, deleting embodiments directed to delivering proteins.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 15, 16 and 19-21 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had

possession of the claimed invention. The final Written Description Examination guidelines that were published on January 5, 2001 (66 FR 1099; available at http://www.uspto.gov/web/menu/).

Specifically, the embodiment of a functional equivalent or functional fragment fails to meet written description. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111 (Fed. Cir. 1991), clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1117. The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed."*Vas-Cath Inc. v. Mahurkar*, 19USPQ2d at 1116. In the instant case, the activities of the encoded protein is described in the claim as being "**capable** of causing apoptosis", however as taught in the instant specification the activity and the ability of even the specific sequences set forth in SEQ ID NOs: 1 and 9 depend on the cell to which they are delivered. Further, it is noted that the activity is described by a circular definition wherein one has to test the material to see if it would cause apoptosis to know if the polynucleotide used meets the limitations encompassed by the claims. The specification teaches that the specific polynucleotide sequences SEQ ID NO: 1 and 9 can cause apoptosis in certain cells in a specific context, however the specification fails to provide any clear guidance to other genes encompassed by the limitation of functional equivalent or a functional fragment thereof, and further, fails to provide the necessary context, i.e. cell type, cell status, other required gene expression, to determine this limitation. Additionally, the specification fails to adequately

describe what a therapeutic gene for the use in treating the specific diseases encompassed by claims 19-21. The claimed invention as a whole is not adequately described if the claims require essential or critical elements which are not adequately described in the specification and which are not conventional in the art as of Applicants effective filing date. Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics (as it relates to the claimed invention as a whole) such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. *Pfaff v. Wells Electronics, Inc.*, 48 USPQ2d 1641, 1646 (1998). In the instant case, Applicants have asserted a specific activity encompassing a large number of polynucleotide sequences, however the specification fails to describe the relevant identifying characteristics of any of the nucleic acid sequences of a representative number of genes or a specific methodology which can be used to define the sequences encompassed by the instantly claimed methods. The skilled artisan cannot envision all the possible sequences or the specific context in which any of these sequences function, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method used. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of identifying it. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (Fed. Cir. 1991).

Further, Applicants attention is drawn to the decision of *The Regents of the University of California v. Eli Lilly and Company* (CAFC, July 1997) wherein it was stated:

In claims involving chemical materials, generic formulas usually indicate with specificity what the generic claims encompass. One skilled in the art can distinguish such a formula from others and can identify many of the species that the claims encompass. Accordingly, such a formula is normally an adequate written description of the claimed genus. In claims to genetic material, however, a generic statement such as "vertebrate insulin cDNA" or "mammalian cDNA," without more, is not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See *Fiers,* 984 F.2d at 1169-71, 25 USPQ2d at 1605-06 (discussing *Amgen*). It is only a definition of a useful result rather than a definition of what it achieves as a result. Many such genes may achieve that result. ***The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention (emphasis added)*** *See In re Wilder*, 736 F.2d 1516, 222 USPQ 369, 372-373 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481, 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence. In the instant case, the recitation of "functional equivalent" and "functional fragment" and the assertion of being capable of inducing apoptosis does not provide adequate description for the

broad array of genes encompassed by the limitation, thus the claims fails to meet the written description requirement under 35 U.S.C. 112, first paragraph.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 15, 16 and 19-21 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 16 and 21 are confusing in the recitation of "said apoptosis is p53-independent" because it does not appear to further limit the independent claims, and only describes the function of delivering the polynucleotide when practicing the method. Claims 16 and 21 do not set forth or encompass any further method steps, and do not further limit the method specifically set forth in claims 15 and 19. More clearly setting forth method steps which differentiate the method for p53-dependent and/or p53-independent forms of apoptosis would obviate the basis of the rejection.

Claims 15 and 19 are unclear and indefinite in the recitation of "capable of inducing apoptosis" because the ability to meet this limitation depends on the cell one is using to test this limitation. The specification teaches the ability of SEQ ID NOs: 1 and 9 to induce apoptosis is

cell status dependent, therefore the ability to determine the metes and bounds of the claims can only be determined in a context specific situation. For example, it is not clear if a polynucleotide which does not induce apoptosis in one cell type would be encompassed by the claim if it is later shown what specific cell cycle status is required for the polynucleotide to induce apoptosis in a particular cell type. The metes and bounds are indefinite because the limitation can vary depending on the cell used to test the limitation encompassed by the claims. Dependent claims are included in the rejection because they fail to further clarify the metes and bounds or clarify the basis of the rejection.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Zhuang *et al.*

The basis of this rejection focuses on the limitation of inducing apoptosis in a cell *in vitro* with a functional equivalent of SEQ ID NO: 1 or SEQ ID NO: 9. In the instant case, the

limitation of functional equivalent is being interpreted broadly to encompass any polynucleotide sequence capable of inducing apoptosis (claim 15) in a p53-independent manner (claim 16). Zhuang *et al.* teach that VP3, termed apoptin, is a protein capable of inducing p53-independent apoptosis in human osteosarcoma cells (see summary in abstract and page 486, bottom of first column). Using the plasmid vector pCAV-tr, Zhuang *et al.* transfect cells and express full length and truncated forms of apoptin in Saos cells (page 488, see figure 4C), which induces increasing amounts of apoptosis in said cells when the protein is present (page 487, figures 1-3 and page 488, figures 4A and B). Finally, Zhuang *et al.* teach that the apoptosis occurs in a p53-independent manner by expressing the protein in p53 negative cell lines (page 487, bottom of second column).

Claims 15 and 16 are rejected under 35 U.S.C. 102(b) as being anticipated by Oorschot *et al.*

The basis of this rejection focuses on the limitation of inducing apoptosis in a cell *in vitro* with a functional equivalent of SEQ ID NO: 1 or SEQ ID NO: 9. In the instant case, the limitation of functional equivalent is being interpreted broadly to encompass any polynucleotide sequence capable of inducing apoptosis (claim 15) in a p53-independent manner (claim 16). Oorschot *et al.* teach that apoptin is a protein capable of inducing p53-independent apoptosis in various human tumor cells (see summary in abstract). Using the plasmid vector pCAV-fs, Oorschot *et al.* transfect cells and express a full length form of apoptin in various tumor cells

(page 5844, see figure 1), which induces increasing amounts of apoptosis in said cells when the protein is present (page 5845, figure 2). Oorschot *et al.* also teach that truncated forms of apoptin is capable of inducing apoptosis in various cell lines as well (page 5845, figure 2). Finally, Oorschot *et al.* teach that the apoptosis occurs in a p53- independent manner by expressing the protein in p53 negative cell lines (page 5846, middle of second column).

Claims 15, 16 and 19-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Pietersen *et al.*

The basis of this rejection focuses on the limitation of inducing apoptosis in a cell with a functional equivalent of SEQ ID NO: 1 or SEQ ID NO: 9. In the instant case, the limitation of functional equivalent is being interpreted broadly to encompass any polynucleotide sequence capable of inducing apoptosis (claims 15 and 19) in a p53-independent manner (claim 16 and 21). Pietersen *et al.* teach that apoptin is a protein capable of inducing p53-independent apoptosis in various human tumor cells (see summary in abstract). Using the adenoviral vector AdMLPvp3, Pietersen *et al.* transduce cells and express a full length form of apoptin in various tumor cells (page 883, see figure 1). Additionally using the adenovirus vector, Pietersen *et al.* demonstrate that delivery and expression of apoptin in a subject is capable of having an antitumor effect on human hepatoma cells in vivo (pages 886-887, starting at the bottom of first column and results in figure 7). Finally, Pietersen *et al.* teach that the apoptosis occurs in a p53-

independent manner in summarizing the previous work of others characterizing the properties of apoptin (page 889, top of first column).

Conclusion

No claim is allowed.

The present specification provides evidence that AAP-5 and mutants thereof are capable of inducing a p53 independent apoptosis in transformed cells. The sequences encoding AAP-5, SEQ ID NOs: 1 and 9, are free of the art of record, however the breadth of the present claims encompass the use of other polynucleotide sequences which are anticipated.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach whose telephone number is (703)305-3732.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Reynolds, can be reached at (703)305-4051.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group analyst Dianiece Jacobs whose telephone number is (703) 308-2141.

Papers related to this application may be submitted by facsimile transmission. Papers should be faxed via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers

must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center numbers are (703)308-4242 and (703)305-3014.

Joseph T. Woitach

Anne-Marie Falk

ANNE-MARIE BAKER
PATENT EXAMINER